

involve incubating at least a first nucleic acid and a second nucleic acid, and the first nucleic acid may be operatively associated with an affinity tag, and the second nucleic acid may be operatively associated with a detection tag. The topoisomerase-modulating compound may be a topoisomerase inhibitor or an activator. The topoisomerase may be a Type I, Type II, Type III or Type IV topoisomerase. The screening assay may be performed on a solid support or in a liquid phase. The nucleic acid and topoisomerase may be covalently complexed, wherein the topoisomerase retains its religation activity.

Please replace the paragraph at page 4, line 7-11 with the following paragraph:

The present invention also provides a high-throughput method of screening compounds capable of modulating nucleic acid-modifying enzymatic activity by incubating at least a first nucleic acid, a nucleic acid-modifying enzyme and a potential enzyme-modulating compound, wherein the nucleic acid [hss] has at least one tag, and assaying for nucleic acid religation or cleavage.

#### **In the Claims**

Please substitute the claim set in the appendix entitled Clean Version of Pending Claims for the previously pending claim set. The specific amendments to individual claims are detailed in the following marked up set of claims for the Examiner's convenience.

1. (Amended) A high-throughput method of screening compounds capable of modulating topoisomerase activity comprising:
  - (a) incubating at least a first nucleic acid, a topoisomerase and a potential topoisomerase-modulating compound, wherein the nucleic acid comprises at least one tag, and
  - (b) assaying for a nucleic acid religation product.